REMARKS

Reconsideration and withdrawal of the rejections of the pending claims are respectfully requested in view of the amendments and remarks herein, which place the application in condition for allowance.

I. STATUS OF CLAIMS AND FORMAL MATTERS

Claims 1-11 are under consideration in this application. Claims 1, 7 and 11 have been amended solely to expedite prosecution of the pending claims and for clarity. Support for the amendments can be found throughout the specification and in the claims as originally filed. No new matter has been added.

The Examiner is thanked for withdrawing the rejection under 35 U.S.C. § 112, second paragraph.

It is submitted that the claims, herewith and as originally presented, are patentably distinct over the prior art cited in the Office Action, and that these claims were in full compliance with the requirements of 35 U.S.C. § 112. It is submitted that the amendments of the claims, as presented herein, are not made for purposes of patentability within the meaning of 35 U.S.C. §§ 101, 102, 103 or 112. Rather, these amendments and additions are made simply for clarification and to round out the scope of protection to which Applicants are entitled.

Furthermore, the present amendments to the claims do not add any subject matter that has not already been considered by the Examiner. Therefore, Applicants respectfully request entry of the amendments and reconsideration of the claims.

The issues raised by the Examiner in the Office Action are addressed below in the order they appear in the prior Action.

II. THE REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, ARE OVERCOME

Claim 11 stays rejected under 35 U.S.C. § 112, first paragraph, as allegedly providing no enablement for the prevention of infection of cattle with *Cooperia* or *Ostertagia*, while being enabling for a method of treating infections of cattle with *Cooperia* or *Ostertagia* through the administration of the formulation.

Although Applicants do not agree with the Office Action, in the interest of expediting prosecution, claim 11 has been amended for clarity to replace "treating or preventing infection" with "treating cattle infected with", thereby obviating the rejection.

Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph, are respectfully requested.

III. THE REJECTIONS UNDER 35 U.S.C. § 112, SECOND PARAGRAPH, ARE OVERCOME

Claims 1-11 are rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as invention.

The Examiner contends that claim 1 is vague and indefinite because it is not clear whether the claimed stable formulation comprises at least one active selected from the group consisting of avermectins, milbemycins, and levamisole, wherein the active agent is dissolved in pyrrolidone solvent or the claimed stable formulation comprises levamisole, and at least one active selected from the group consisting of avermectins and milbemycins, wherein the active agents are dissolved in a pyrrolidone solvent.

Although Applicants do not agree with the rejection, in the interest of expediting prosecution, claim 1 has been amended to recite that the formulation comprises a combination of two active ingredients and a pyrrolidone solvent, wherein the said combination of two active ingredients consists of levamisole and an avermectin or levamisole and a milbemycin. Amended claim 1 clearly recites that the formulation requires two actives, wherein one of the active agents is levamisole and the other one is an avermectin or a milbemycin.

Applicants respectfully submit that the amendment to claim 1 overcomes the rejection under 35 U.S.C. § 112, second paragraph.

Therefore, reconsideration and withdrawal of the rejections under 35 U.S.C. §112, second paragraph, are respectfully requested.

IV. THE REJECTIONS UNDER 35 U.S.C. §102 ARE OVERCOME

Claims 1, 3-5 and 7-10 remain rejected under U.S.C. §102(b) as allegedly being anticipated by Komer (U.S. Patent No. 5,773,422).

Claims 1, 3-8, and 10 are rejected under 35 U.S.C. §102(b) as allegedly being anticipated by Sorensen et al. (WO 01/05232). Applicants respectfully traverse the rejections.

It is respectfully pointed out that a two-prong inquiry must be satisfied in order for a Section 102 rejection to stand. First, the prior art reference must contain all of the elements of the claimed invention. *See Lewmar Marine Inc. v. Barient Inc.,* 3 U.S.P.Q.2d 1766 (Fed. Cir. 1987). Second, the prior art must contain an enabling disclosure. *See Chester v. Miller,* 15 U.S.P.Q.2d 1333, 1336 (Fed. Cir. 1990). A reference contains an enabling disclosure if a person of ordinary skill in the art could have combined the description of the invention in the prior art reference with his own knowledge of the art to have placed himself in possession of the invention. *See In re Donohue*, 226, U.S.P.Q. 619, 621 (Fed. Cir. 1985).

The Examiner's rejection of claims 1, 3-5 and 7-10 under U.S.C. §102(b) as being anticipated by Komer is based on the Examiner's interpretation of claim 1 as listing levamisole as a part of a Markush group also consisting of avermectins and milbemycins. Office Action at 8.

Although Applicants do not agree with the Examiner's interpretation of claim 1, in the interest of expediting prosecution, claim 1 has been amended for clarity according to the Examiner's suggestions (Office Action at 18-19). Claim 1 as amended clearly recites that the novel formulation requires a combination of levamisole and an avermectin or a milbemycin.

Komer relates to the formulations comprising an avermectin or an avermectin and Clorsulon, but does not teach or suggest the use of levamisole in the said formulations. As such, the reference does not contain all the elements of claimed invention, and therefore does not anticipate the instant claims.

The Examiner alleges that the teachings of Sorensen et al. describing a stable veterinary composition of benzimidazole in lactic acid, where N-methyl-2-pyrrolidone is present as a co-solvent (page 3, line 29) and an example of a composition comprising abamectin, levamisole HCl, triclabendazole and other ingredients destroy the novelty of claims 1, 3-8, and 10.

Solely to expedite prosecution, claim 1 has been amended to clarify that the formulation comprises a combination of two active ingredients and a pyrrolidone solvent, wherein the said combination of two active ingredients consists of levamisole and an avermectin or levamisole and a milbemycin. Sorensen et al. does not teach or suggest the use of levamisole in

combination with an avermectin or milbemycin in the absence of benzimidazole and lactic acid. As such, the reference does not anticipate the claimed invention.

In view of the foregoing, reconsideration and withdrawal of the rejections under 35 U.S.C. § 102(b) are respectfully requested.

V. THE REJECTIONS UNDER 35 U.S.C. § 103(a) ARE OVERCOME

Claims 1 and 2 remain rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Komer (U.S. Patent No. 5,773,422) in view of Huet et al. (U.S. Patent No. 6,426,233) and Harvey (U.S. Patent No.6,165,987).

Claims 1 and 6 remain rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Komer (U.S. Patent No. 5,773,422) in view of and Harvey (GB Patent Application No. 2252730).

Claims 1 and 11 remain rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Komer (U.S. Patent No. 5,773,422) in view of Harvey (U.S. Patent No.6,165,987).

Claim 2 is rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Sorensen et al. (WO 01/05232) as applied to claims 1, 3-8, and 10, and in further view of Huet et al. (U.S. Patent No. 6,426,233) and Harvey (U.S. Patent No.6,165,987).

Claim 9 is rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Sorensen et al. (WO 01/05232) as applied to claims 1, 3-8, and 10, and in further view of Komer (U.S. Patent No.5,773,422).

Claim 11 is rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Sorensen et al. (WO 01/05232) as applied to claims 1, 3-8, and 10, and in further view of Harvey (U.S. Patent No.6,165,987).

Applicants respectfully disagree and traverse the rejections.

The Examiner is respectfully reminded of the case law, namely, that there must be some prior art teaching which would have provided the necessary incentive or motivation for modifying the reference teachings. *In re Laskowski*, 12 U.S.P.Q. 2d 1397, 1399 (Fed. Cir. 1989); *In re Obukowitz*, 27 U.S.P.Q. 2d 1063 (BOPAI 1993). As stated by the Court in *In re Fritch*, 23 U.S.P.Q. 2d 1780, 1783-1784 (Fed. Cir. 1992): "The mere fact that the prior art may be modified in the manner suggested by the Office Action does not make the modification obvious unless the

prior art suggests the desirability of the modification." Also, the Examiner is respectfully reminded that for the Section 103 rejection to be proper, both the suggestion of the claimed invention and the expectation of success must be founded in the prior art, and not Applicants' disclosure. *In re Dow*, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988).

Furthermore, the Supreme Court has recently reaffirmed the factors set out in *Graham v. John Deere Co. of Kansas City*, 383 U.S. 1, 17-18: "[T]he scope and content of the prior art are determined; differences between the prior art and the claims at issue are...ascertained; and the level of ordinary skill in the pertinent art resolved. Against this background the obviousness or nonobviousness of the subject matter is determined. Such secondary considerations as commercial success, long felt but unsolved needs, failure of others, etc., might be utilized to give light to the circumstances surrounding the origin of the subject matter sought to be patented." *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727.

Applying the law to the instant facts, the references relied upon by the Office Action do not disclose, suggest or enable Applicants' invention. The cited references do not teach or suggest the formulations that contain levamisole in combination with at least one avermectin or milbemycin to treat the cattle parasites, and in particular, to overcome parasite resistance, in *Cooperia* or *Ostertagia*, as recited in the pending claims as amended.

The Examiner's rejection of claims 1, 2, 6 and 11 under 35 U.S.C. § 103(a) as being unpatentable over Komer (U.S. Patent No. 5,773,422) in view of Huet et al. (U.S. Patent No. 6,426,233), Harvey (U.S. Patent No.6,165,987) and Harvey (GB Patent Application No. 2252730) is based on the Examiner's interpretation of claim 1 as listing levamisole as a part of a Markush group also consisting of avermectins and milbemycins. Office Action at 11-12.

Although Applicants do not agree with the Examiner's interpretation of claim 1, in the interest of expediting prosecution, claim 1 has been amended for clarity. Claim 1 as amended clearly recites that the claimed formulation requires a combination of two active ingredients, levamisole and an avermectin or levamisole and a milbemycin.

Applicants respectfully submit that neither Komer nor Huet et al. or Harvey teaches or suggests the incorporation of levamisole. Komer relates to the formulations comprising an avermectin or an avermectin and Clorsulon, but does not teach or suggest combining an avermectin with levamisole.

Furthermore, the reference does not relate to the stability of a formulation containing a combination of an avermectin and levamisole in pyrrolidone solvent. It is well known in the art that avermectin compounds may be unstable at certain pH ranges (for example, see paragraphs [0018] and [0022] of the published application). It is also known that incorporation of other active agents may adversely impact the stability of formulations containing avermectin compounds. Therefore, the stable formulation recited in the claims as amended cannot be predicted or expected based on Komer, Huet or Harvey, either alone or in combination. As such, and in view of the arguments presented in the response to the previous Office Action, neither Komer nor Huet et al. or Harvey, alone or in combination, renders the instant claims obvious.

The Examiner alleges that it would have been *prima facie* obvious to an ordinary skilled artisan at the time the instant invention was made to modify the formulation of Sorensen et al. described as a stable veterinary composition of benzimidazole in lactic acid, where N-methyl-2-pyrrolidone is present as a co-solvent (page 3, line 29) and further exemplified as a composition comprising abamectin, levamisole HCl, triclabendazole and other ingredients, by incorporating additional solvents like glycol ethers as taught by Huet et al., because Harvey discloses that the anthelmintic agents need to be administered as solutions by dissolving them in solvents such as ethers to be bioavalable.

Applicants respectfully submit that establishing a *prima facie* case of obviousness requires that the prior art reference must teach or suggest all the claim limitations.

The reference by Sorensen et al. relates to a veterinary composition where a benzimidazole is carried in lactic acid and teaches that lactic acid is required to dissolve benzimidazoles and provide good longer term homogeneity as well as good chemical stability (page 3, lines 13-16 of WO 01/05232) and that the inclusion of N-methyl-2-pyrrolidone is optional (page 4, lines 16-20). Therefore, the reference does not teach or suggest the use of a pyrrolidone solvent alone to provide a stable formulation of levamisole and an avermectin or milbemycin and furthermore, does not show the desirability of such formulation. The reference also does not relate to the stability of such formulation containing a combination of levamisole and another active selected from avermectins or milbemycins in pyrrolidone solvent in the absence of lactic acid.

Contrary to the Examiner's allegations, there is no teaching, suggestion or motivation in Sorensen et al. to modify the described composition of benzimidazole in lactic acid to prepare

the claimed formulation of a pyrrolidone solution of levamisole and an avermectin or milbemycin in the absence of benzimidazole and lactic acid. As noted above, it is known that formulations comprising avermectins require certain pH ranges and may be adversely affected by inclusion of additional active agents. As such, the stability of formulations comprising an avermectin compound in combination with another active agent cannot be predicted and would not be obvious in view of Sorensen.

Huet *et al.* relates to the use of 1-phenylpyrazoles in combination with macrocyclic lactone anthelmintic agents and does not teach or suggest the use of levamisole in such formulations.

Harvey relates to the use of praziquantel in combination with macrocyclic lactone anthelmintic agents and does not teach or suggest the use of levamisole in such formulations.

Komer relates to an injectable formulation for administration of avermectin, and does not teach or suggest combining at least one avermectin or milbemycin with levamisole.

Moreover, Komer and Harvey relate to formulations that allow water as a solvent and therefore are teaching away from the present invention.

In view of the foregoing, neither Sorensen et al. nor Huet et al. or Harvey or Komer, alone or in combination, teaches or suggests the invention of pending claims.

The invention of pending claims is directed to the combination of levaimisole and another active selected from avermectins or milbemycins to reduce the potential of parasites to survive the treatment and to the formulation of the said combination with the desired stability and ease of use. Certain parasite species are known to exhibit resistance when treated with benzimidazole compounds or members of avermectin/milbemycin group or levamisole/morantel based treatment (see, for example, paragraphs 0003-0015 of the application as published). As disclosed, the invention provides a stable formulation that can successfully treat the cattle parasite species and infections caused by these species, in particular by Cooperia, which is the key dose limiting parasite of the avermectin/milbemycin group and Ostertagia, which is a limiting parasite of levamisole, by combining the effective amounts of at least one avermectin or milbemycin and levamisole in a pyrrolidone solvent.

Therefore the presently claimed formulation is highly advantageous as it provides the desired efficacy and prevents parasite's resistance to the treatment. It has been shown that the claimed combination of actives exhibits outstanding efficacy against all parasite species (p. 8,

paragraphs 0107-0110 of the specification as published) and successfully resolves the problem of anthelmintic resistance.

Contrary to the Examiner's assertions, one of ordinary skill in the art would not be able to modify the formulation of Sorensen et al. in view of other cited references to derive the formulation of the instant claims.

As such, the cited references do not render the pending claims *prima facie* obvious. Accordingly, reconsideration and withdrawal of the rejections under 35 U.S.C. § 103(a) are respectfully requested.

CONCLUSION

Reconsideration and withdrawal of the rejections of the application are respectfully requested in view of the remarks and amendments herein, and prompt issuance of a Notice of Allowance is respectfully requested.

If the Examiner believes any informalities remain in the application, which may be corrected by Examiner's amendment, or whether any other issues can be resolved by telephone interview, a telephone call with the undersigned attorney is courteously solicited.

Respectfully submitted,
MERIAL LTD.
FROMMER LAWRENCE & HAUG LLP

By: 

Judy Jarecki-Black, Ph.D.
Reg. No. 44,170
Tel. No. (678) 638-3805
Fax No. (678) 638-3350
Thomas J. Kowalski
Reg. No. 32,147
Deborah L. Lu
Reg. No. 50,940
Tel. No. (212) 588-0800
Fax No. (212) 588-0500